The clinical significance of this lesion is in its distinction from peptic disease or malignancy of the stomach, and in its propensity for upper gastrointestinal tract obstruction.

The distinction from peptic disease and carcinoma is supported by evidence of regional enteritis elsewhere in the gastrointestinal tract.[10,11] Further support is obtained from findings on gastric cytology, endoscopy and biopsy.[12] Occasionally laparotomy may be necessary to establish the diagnosis. The case reported by Dr. Burbige illustrates the difficulty in distinguishing Crohn's disease from carcinoma. The value of endoscopic biopsy was shown only in retrospect but serves to illustrate the potential of this procedure for definitive diagnosis in this form of the disease.

Repeat gastroscopy one year after diagnosis in this case showed remarkable improvement. The potential for improvement, either as the natural course of the disease or as a consequence of medical therapy, encourages a conservative approach to this problem. In those instances of refractory obstruction, a bypass surgical procedure has been successful in relieving the obstruction.[13] The reluctance toward early and extensive surgical operation in any patient with Crohn's disease becomes more reasonable when one reviews the results of operations in Crohn's disease. One is discouraged by the reported recurrence rate of approximately 50 percent.[9] Data such as these tend to discourage surgical management of Crohn's disease unless it is compelled by serious complications or a deteriorating course of the illness.

The reported improvement in Dr. Burbige's patient affords the opportunity to speculate on the relationship of the therapy and the possible cause of this disease. Could there have been response in this patient to the antimicrobial and adrenal steroid therapy? Several authors have reported on the possibility of infection as a cause of this disease. There are reports of the induction of histopathological changes similar to those of Crohn's disease in experimental animals.[14,15] Electron microscopic studies have been reported to show microorganisms in the lamina propria and submucosa of diseased colon with Crohn's disease.[16] The isolation of bacterial variants of pseudomonas from tissues involved with Crohn's disease has been reported.[17] Viral isolation and a tissue culture system enabling replication and characterization of a virus isolated from tissue involved with Crohn's disease have also been reported.[18,19]

Although these findings are at variance, the efforts are encouraging and show promise of eventually understanding the cause of this disease.

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Testicular Tumors

ELSEWHERE IN THIS ISSUE appears a timely Specialty Conference on testicular tumors. In recent years great advances have been made in our understanding of these tumors but much work remains to be done in epidemiology, detection and diagnosis, and pathology and treatment.

Three aspects of epidemiology deserve mention. While the annual age-adjusted incidence rates for all races is three per 100,000, Twito and Kennedy[1] have shown that in the 15- to 34-year-old age group testicular tumors are the most frequent malignancy. In men 35 to 59 years old, while lung tumors take precedence, testicular tumors account for seven per 100,000, which is more than double the rates in the general population.

A doubling of morbidity rate has been reported in comparing the 1943-1947 period with the 1958-1962 period (Clemmesen).[2] A similar trend in the United States has been suggested by Grumet and McMahon.[3] Testicular tumors are extremely rare among blacks under the age of 45 with the ratio of about one to six in comparison with whites. No comprehensive study of environmental factors responsible for these observations has been carried out.

Compared with the publicity about breast examination in women, to date no effort has been made to alert young men to examine their scrotums for a nodule, enlargement or change in consistency. Men rarely feel their scrotums and if there is any abnormality the patient is reluctant to consult a physician. Once he has consulted a physician there is often a long delay in orchiectomy with tragic consequences for the patient. Borski has called attention to the fact that there is a six-month delay between diagnosis and treatment.[4]

The clinical classifications used in the United States have almost completely ignored the local extent of the tumor and tumors confined to the scrotum have generally been categorized as stage A. The International Union Against Cancer (Union Internationale Contre Cancer, or UICC) has had a Commission on Clinical Stage Classification of Tumors, headed in succession by Dr. Perry (USA), Prof. Denoix (France), Mr. Harmer (UK) and Prof. van der Werf (Holland). This commission has had several subcommittees on urological tumors and has published a clinical classification of these tumors which has been adopted by the American Joint Committee on Clinical Stage Classification of Tumors:

UICC Clinical Classification of Testis Tumors

T1 - Tumor limited to the body of the testis
T2 - Tumor extending beyond the tunica albuginea
T3 - Tumor involving the rete testis or epididymis
T4 - Tumor invading the spermatic cord and/or scrotal wall
  T4a - Invasion of spermatic cord
  T4b - Invasion of scrotal wall

The details of this classification are available in a UICC publication[5] and a report by Mr. David Wallace.[6] It should be noted that the T categories of UICC are subclassifications of stage A of Dr. Thompson's as presented in this conference.

The first serious effort to classify testicular tumors according to histology was made by Friedman and Moore.[7] This was, in fact, Dr. Friedman's classification and, happily, he has been a participant in the conference. Friedman and Moore's study was followed by a report by Dixon and Moore,[8] who correlated pathology with behavior. In the report of survival and mortality of patients with testis tumors these authors grouped the tumors into five categories: pure seminoma; embryonal carcinoma with or without seminoma; teratoma pure or with seminoma; teratoma with either embryonal carcinoma or choriocarcinoma or both, and with or without seminoma; choriocarcinoma pure or with seminoma or embryonal carcinoma or both. This classification has resulted in some confusion because it has been interpreted as a histological classification which it was not intended to be. Mostofi (1973)[9] modified this classification emphasizing the need for precise identification and listing of each element in the tumor. In the meantime the situation has become more complicated by the fact that there also have developed British, French and Russian pathological classifications. Since these classifications cannot be equated with each other it has been impossible to compare incidence and prevalence rates, survival and mortality rates and results of therapy.

The World Health Organization (WHO), in its program of arriving at standard classifications of tumors of various sites, has endeavored to create a standard histopathological classification of testis tumors. Understandably, the problem was quite difficult to solve because pathologists tend to become emotional about any classification they happen to use. To WHO's credit it should be said that all the protagonists, including Prof. Cabanne (France), Prof. Ganina (USSR), Dr. Mostofi (USA), Dr. Pugh (UK), Prof. Teilum (Denmark) and a number of other pathologists were brought together and after two conferences a simple classification based entirely on histology was devised. The details of classification have been published by WHO (1977).[10]

The WHO classification[10] subdivides germ cell tumors into tumors of a single histological pattern and those with more than one histological pattern. The former includes seminoma, spermatocytic seminoma, embryonal carcinoma, yolk sac tumor (embryonal carcinoma, infantile type), pure choriocarcinoma and teratoma. Teratoma may be mature or immature, or teratoma with malignant areas not recognizable as any of the above but with squamous cell carcinoma, adenocarcinoma

or carcinoid, and so forth. In about 40 percent of germ cell tumors more than one histological type is present. The WHO classification recommends that the specific histological types be listed; for example, teratoma and embryonal carcinoma, choriocarcinoma and teratoma.

It may well be asked why we should have a new pathological classification. Actually, the WHO classification is not a new classification. It is a more systematic listing and more precise definition of the major basic histological types—seminoma, embryonal carcinoma, choriocarcinoma and teratoma—and whether they occur in pure form or admixtues and, if so, the precise types that are present. Two other histologic types are also listed—spermatocytic seminoma and yolk sac tumor—but these are rarely seen in young men.

It may be argued that by the time an investigator classifies his cases according to this classification the number in each category will be too small for statistical purposes. But the structure, behavior and treatment of each of these main categories (seminoma, embryonal carcinoma, choriocarcinoma and teratoma) are so different that any pathological classification that lumps any of these together is worthless. The WHO effort in subdividing teratomas into mature and immature teratoma is especially desirable because we do not know whether there is any difference in the behavior of these two categories which have, to date, been buried under teratoma.

Since 40 percent of testicular tumors show more than one histological pattern and a tumor of one pattern may show a totally different pattern in the metastasis, it is essential that the orchiectomy specimen be thoroughly investigated not only in the neoplastic but in nonneoplastic areas as well. Furthermore, the remaining wet tissue should be saved for at least seven years. This is highly desirable because if late metastasis of a different pattern develops in a patient, one can go back to the original primary specimen for possible explanation of the apparent dichotomy.

Some work is being done on histological demonstration of chorionic gonadotropins and alpha fetoproteins on fixed tissue. But there is great need for application of modern techniques of histology to these tumors: histochemistry, tissue culture, fluorescence microscopy, transmission and scanning electron microscopy. These techniques require immediate and proper handling of the specimen.

One of the most important and least studied areas is endocrinology of testicular tumors. The commendable policy of immediate orchiectomy has often resulted in incomplete hormone assays. Spermatic vein blood, which can easily be collected at the operating table after ligation of spermatic artery, yields a more accurate determination of the exact type of hormone produced than does blood from general circulation. Radioimmunoassay has provided a more delicate quantitation of the hormones and this is especially valuable in follow-up of patients after orchiectomy.

Still another area for research is correlation of histology with hormone level. How much chorionic gonadotropin producing tissue must be present to give what level of hormone in the assay. It is essential that the precise structure of the tumor be identified and the components listed and quantitated so that they can be correlated with hormone levels.

The large scale introduction of chemotherapy in treatment of testicular tumors has opened a new era in dealing with these tragic tumors. Embryonal carcinoma, choriocarcinoma and tumors in which these two elements are present are most amenable to chemotherapy, as discussed elsewhere in this Specialty Conference. Here again, the exact histological types of tumor should be listed to alert radiotherapists and chemotherapists of the situation as it exists and to enable them to make proper evaluation of the results as to tumor type and agent.

One area that demands special attention is the discovery of one or more agents that alone or in combination can result in transforming embryonal carcinoma with or without other elements to a mature teratoma which could then be surgically excised.

In conclusion, two points merit emphasis; there is urgent need for standard nomenclature in clinical and pathological diagnosis and classification, and there is great need for research on epidemiology, etiology, structure and behavior of testicular tumors in man.

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Derzon to DHEW

ONCE AGAIN California and the West are sending an unusually able health professional to an important post in the government in Washington. Robert A. Derzon is a skilled and experienced administrator intimately familiar with the heartaches and triumphs of patient care, and the problems and challenges of education and research in the health sciences. He brings his intellect, his warm compassion and his considerable fiscal skills to the Health Care Financing Administration (HCFA), a newly created division of the Department of Health, Education, and Welfare (DHEW), as its first Administrator. He has stated:

> A real issue in this decade will be whether health professionals can set aside their self-interest to concentrate on the ways in which we can increase the health of our population. Hopefully, we can advise our sick patients to become prudent and judicious users of our expensive but vital hospitals and our health care resources. Government and the private sector must coalesce in finding ways to moderate the escalation in health care costs by assuring access to pluralistic and diverse health care systems, while maintaining high standards and humane service.

It is the interest of all concerned to achieve these goals. The nation should be well served with Bob Derzon in a position of leadership to accomplish them. He deserves and will need the help of us all.

—MSMW

Fibrosing Alveolitis

—*Extrinsic Allergic and Cryptogenic*

THE TERM "fibrosing alveolitis" has been coined by John G. Scadding of England as a generic name for the disease that had been described under such names as interstitial pneumonia or pneumonitis, acute or chronic Hamman-Rich disease or syndrome, idiopathic interstitial fibrosis, chronic diffuse sclerosing alveolitis, organizing interstitial pneumonia and usual interstitial pneumonia. Fibrosing alveolitis has been subdivided into two groups: extrinsic allergic alveolitis (typified by farmer's lung) and cryptogenic fibrosing alveolitis. In this country extrinsic alveolitis is referred to as "hypersensitivity pneumonitis"; whereas, cryptogenic fibrosing alveolitis is commonly called "idiopathic pulmonary fibrosis." A number of clinical, radiographic, immunologic and histologic features enable these two forms of "fibrosing alveolitis" to be clearly differentiated.[1]

Extrinsic allergic alveolitis is characterized by an acute or insidious onset of dyspnea, malaise, fever, muscle pains and weight loss. There is a history of frequent and regular inhalation of some organic allergen. Auscultation of the lungs may show fine crepitations. On roentgenograms of the chest, diffuse nodular infiltration with a tendency to involve mid- and upper lung fields may be seen. Fibrosis when it occurs mainly involves the upper lobes. Precipitating antibodies in the serum, belonging to immunoglobulins G (IgG) class, against the relevant allergen are usually present. Analysis of bronchial lavage fluid shows a striking increase in T-lymphocytes and immunoglobulin M (IgM) along with some eosinophils and IgG.[2] In early disease histologic examination of the lung tissue shows noncaseating granulomata, but in the advanced stage, granulomata are replaced by fibrous tissue. Corticosteroids are effective in the early stage before fibrosis is established.

Cryptogenic fibrosing alveolitis or idiopathic pulmonary fibrosis differs from the extrinsic type in many ways. Dyspnea on exertion is the constant symptom but fever, muscle pains and weight loss are absent. Clubbing of the fingers and toes occurs in as many as 70 percent of the patients and crepitant rales are present in more than two thirds of the patients. Radiological appearance varies with the stage and extent of the disease and includes ill-defined patchy opacities, nodular infiltrates, linear and reticular shadows, "ground glass" appearance and honeycombing. Unlike extrinsic allergic alveolitis the roentenographic abnormality is diffuse. Lung function studies show reduction of static lung volumes and diffusing capacity for carbon monoxide but the degree of fibrosis is best correlated with the change in arterial oxygen tension and alveolar-arterial oxygen difference on exercise and the coefficient of lung retraction (maximum static transpulmonary pressure/observed total lung capacity).[3] Immunologic